Dietary Fats & Health

Navigating the Slippery Slope

Ed Cox, M.D.

Fat is good for you

Repeat after me: "Fat in my diet is good for me"

The myth

- USDA, American Heart Assn, American Cancer Society have kept up the drum beat for 30 years that fat is bad for you, especially saturated fats, and should be avoided
- They meant well

The reality

- Data does not support this advice

It is difficult to unlearn a "truth" you've been bludgeoned with for decades

- Yet, you must!
- Fat is not the enemy, and fat-dense foods such as nuts are super-healthy
- Exception: Trans fats (hydrogenated fats) are dangerous and should be avoided

Goal: Become friendly with fat

Accept that dietary fat is not the enemy

Learn fats by name and associate that with their appearance

Be able to read and interpret Nutrition Facts and ingredient labels

Prepare for "Cholesterol" lecture

Fats & Oils - Definition

Fats and oils are substances that do not mix with water and have a slick feeling ("greasy")

Fat generally refers to substances that are solid at room temperature, whereas oils are those that are liquids

Fats and oils are organic compounds, that is, largely or exclusively composed of carbon and hydrogen

This definition would include petroleum and waxes, so clearly not sufficiently specific

Lipids

"Lipids are a group of *naturally* occurring molecules that include fats, waxes, sterols, fat-soluble vitamins (such as vitamins A, D, E, and K), monoglycerides, diglycerides, triglycerides, phospholipids, and others"

Wikipedia

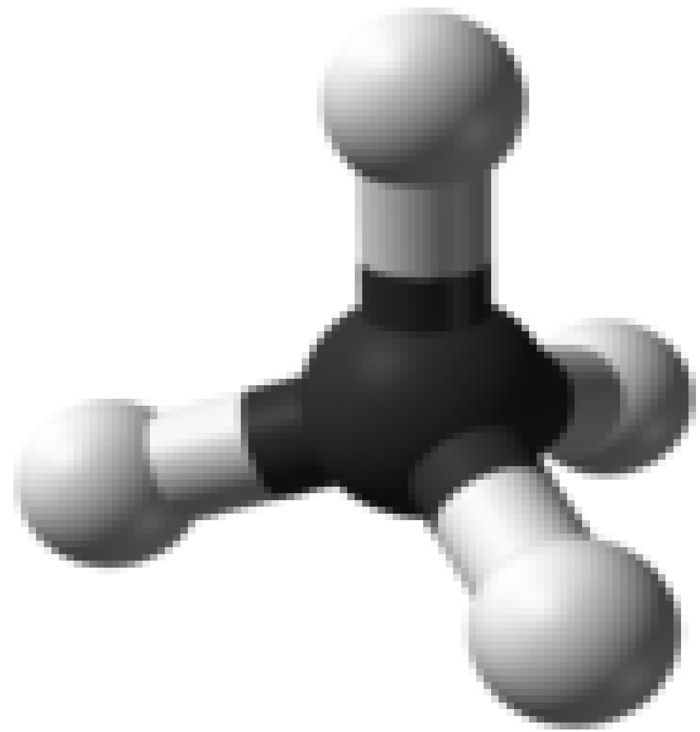
Hydrocarbon compounds

Hydrocarbons are compounds made up of carbon and hydrogen, mostly

Methane (CH_4) is symmetric and has only weak net charges

Methane molecules only weakly attract one another or other molecules

Consequently, methane is a gas at room temperature, while other similar simple compounds (e.g., water) are liquids



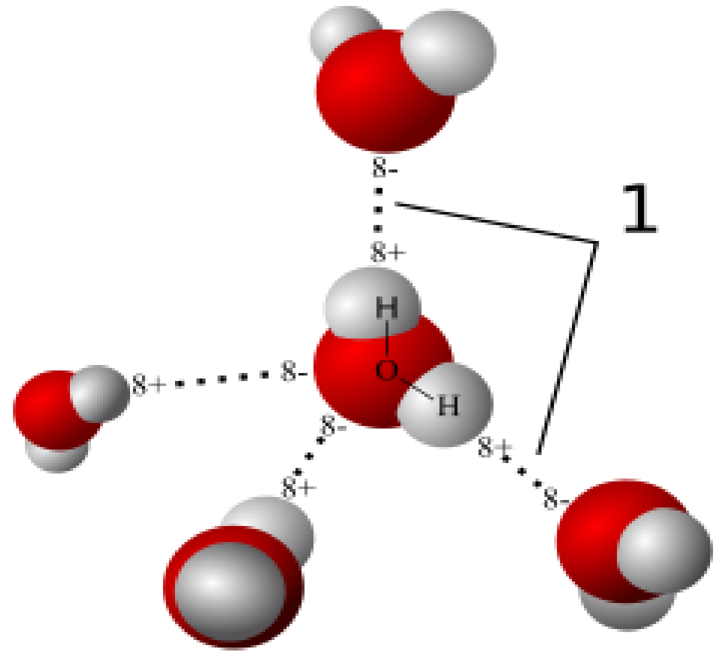
Water-water bonding

Molecules of H_2O strongly attract one another

Due to asymmetry, oxygen (red) has a slight net negative charge; the hydrogens have a slight positive charge

Opposites attract ("hydrogen bonding")

H_2O – a small molecule – is a liquid at room temperature because of this strong attraction



Oil and water

"Oil [lipids] and water do not mix"

Blood is mostly water with other stuff floating around in it

To move lipids around in the blood stream efficiently requires special methods of making them soluble

Oil and water interaction

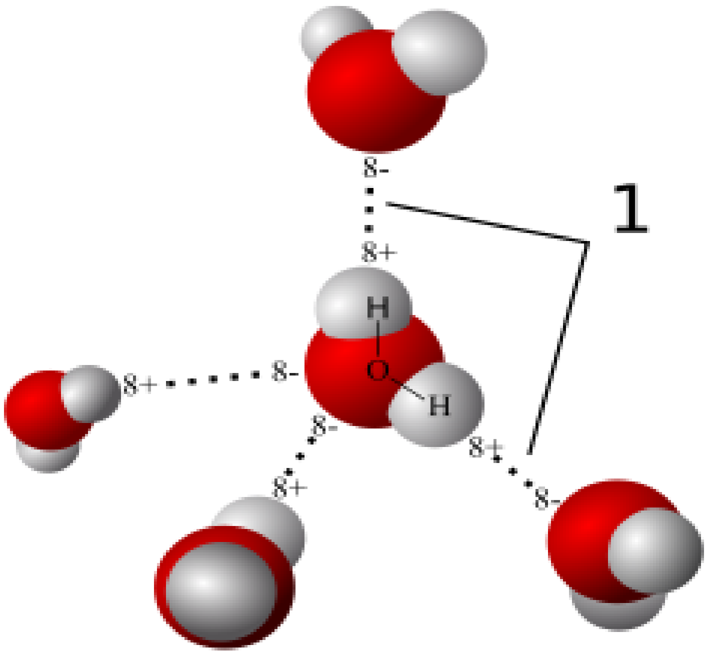
"Oil molecules and water molecules repel"

- Actually water molecules attract one another so tightly that they reject oil molecules
- H_2O molecules' mutual attraction is based on electric charge
- Oil molecules have nowhere to go other than to hang out with other oil molecules

Oil is said to be *hydrophobic* ("water fearing") or *lipophilic* ("fat loving")

Other molecules that mix well with water, such as many proteins, are said to be *hydrophilic*

- They have atoms with net electric charges sticking out to "bond" with H and O

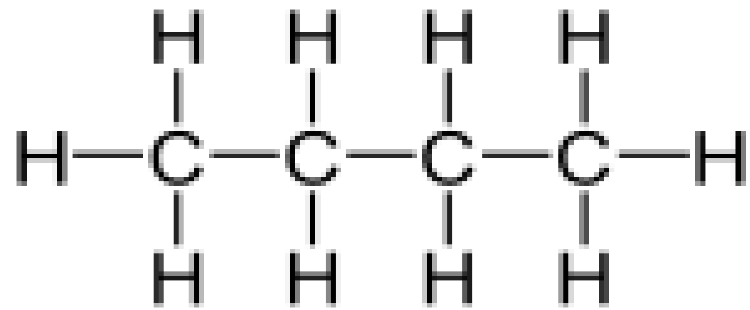


Hydrocarbon compounds can attract and aggregate

Simple carbon compounds are hydrophobic ("water fearing")

If they have enough mutual attraction, they will aggregate together, after separating form water

- Butane is a liquid at room temperature



Hydrocarbons: Alkanes

Hydrocarbons are compounds mostly comprised of carbon and hydrogen in various length chains and combinations with other elements

Alkanes are simplest – just C and H - but don't occur in living organisms, only as fossil fuels

- Octane – eight carbons, 18 hydrogens

Fatty acids and triglycerides

A very common type of oil / fat in Nature is the "fatty acid", abbreviated FA

I will gently introduce fatty acids over the next few slides

Fatty acids are often bound to glycerin for storage

- One glycerin molecule attaches to (up to) three FA molecules
- If the glycerin has 3 FA attached, it is a **tri**glyceride

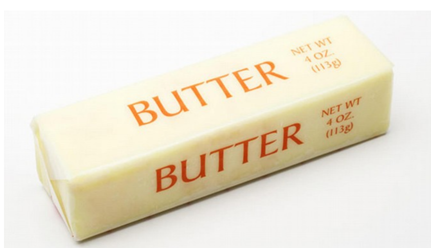
Triglycerides?

Suppose I send you to the store with instructions to bring home some triglycerides

- Will you know what to pick up?

You will now...

Triglycerides!



Basic hydrocarbons

Organic chemistry is carbon chemistry

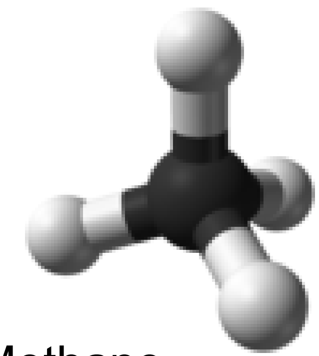
- Carbon is the essential element of all life forms

Hydrocarbons (carbon + hydrogen) are the fundamental organic molecules

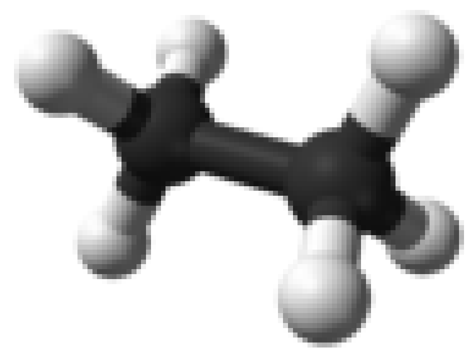
Methane CH_4 is the most basic molecule

- Black = carbon
- White = hydrogen

Ethane C_2H_6 is next most complex



Methane



Ethane

Double bonds

Each carbon can make four bonds

Each ethane carbon makes one bond with the other carbon and one with each of three hydrogens

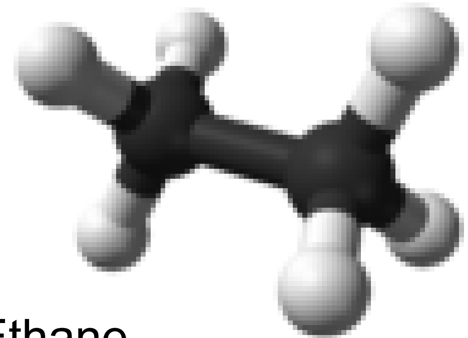
Ethylene (AKA ethene) carbons make *two* bonds with the other carbon and one each with two hydrogens

When two adjacent carbons make two bonds with one another, this is a *double bond*

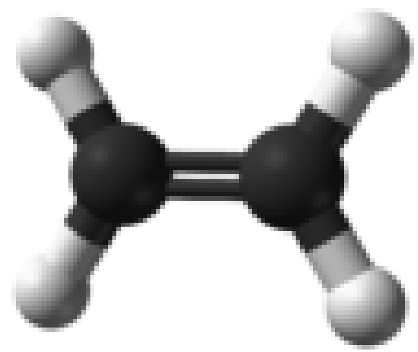
Double bonds make molecules more “rigid”, often creating bends in long chains

The double bond in a molecule can be converted to a single bond by reacting the molecule with hydrogen under the “right” conditions

- Reaction referred to as “saturation”



Ethane



Ethylene

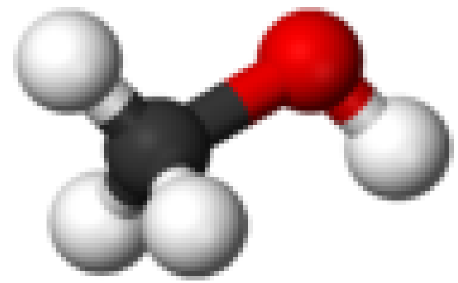
Alcohols – Add OH

Replacing one hydrogen with -OH (hydroxyl group of oxygen and hydrogen) converts alkane into alcohol

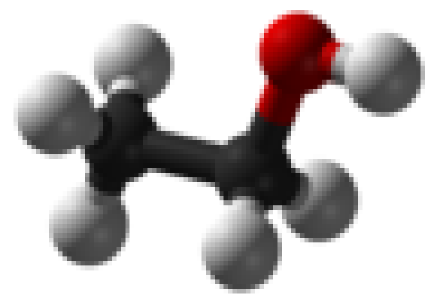
- Red = oxygen

Methane, minus one hydrogen, plus -OH, is methyl alcohol, or methanol, CH_3OH

Ethane, minus one hydrogen, plus -OH, is ethyl alcohol, or ethanol, C_2H_5OH



Methanol



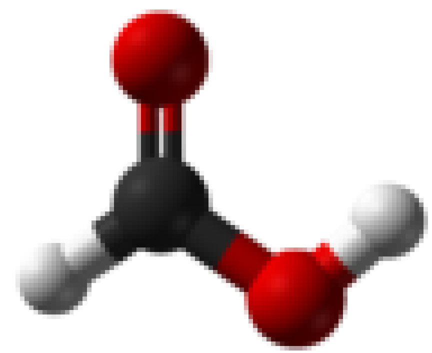
Ethanol

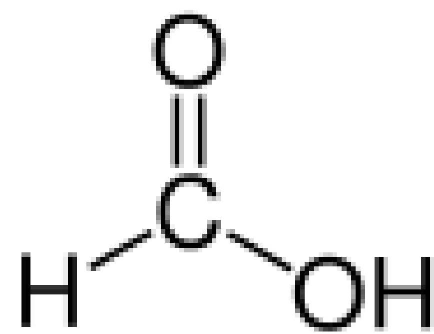
Carboxylic acids - COOH

Carboxylic acids are alkanes in which a terminal carbon has an -OOH group replacing three hydrogens

In simple concept, one oxygen is double bonded to the carbon and an hydroxyl group shares the remaining electron

The simplest carboxylic acid is methanoic acid, better known as formic acid (the stinging chemical injected by ants and other insects when they bite)





Carboxylic acids - COOH

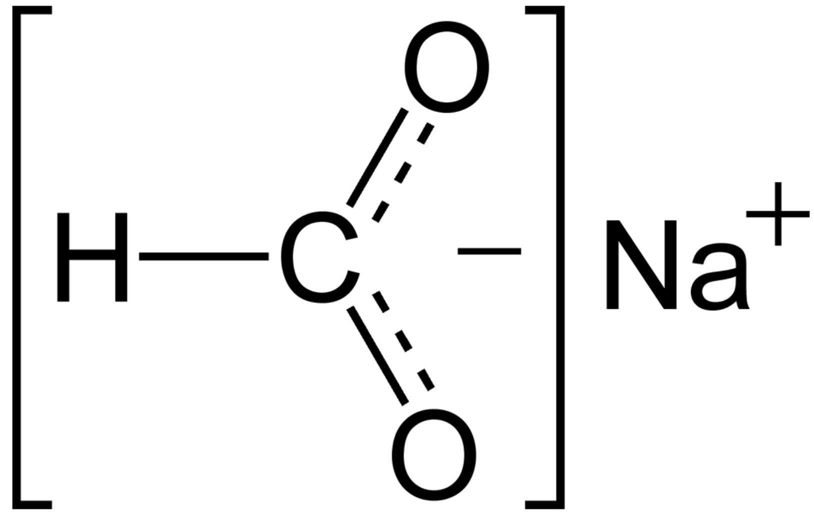
In actuality, the oxygens tug the electron away from the hydrogen and share it between themselves

The hydrogen ion thus formed flies off, leaving the negatively charged formate ion behind

The formate can associate with other positive ions to form salts

- Sodium formate

Carboxylic acids readily enter into reactions involving the oxygen end

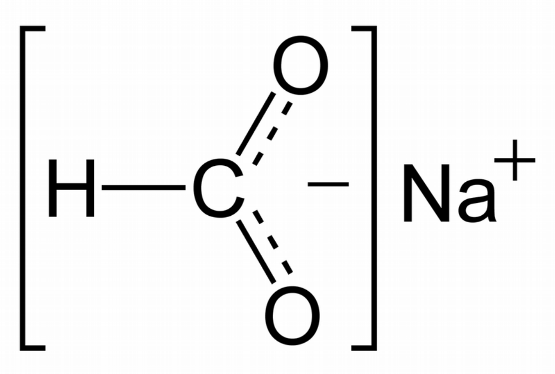


Carboxylic acids - COOH

Carboxylic acids readily enter into reactions involving the oxygen end

A viper is a useful metaphor for a carboxylic acid

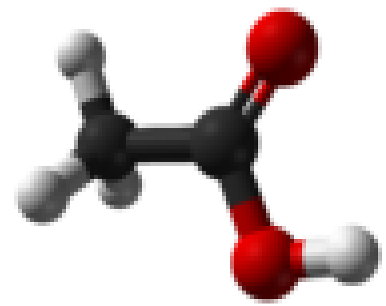
The COO- works like the fangs and jaws of a snake; it aggressively attacks and attaches to a variety of other molecules

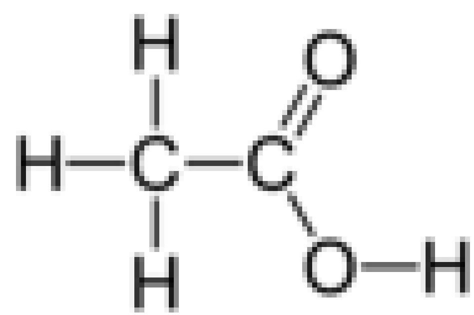


Ethanoic (acetic) acid

The second simplest carboxylic acid - ethanoic acid, or better known as acetic acid

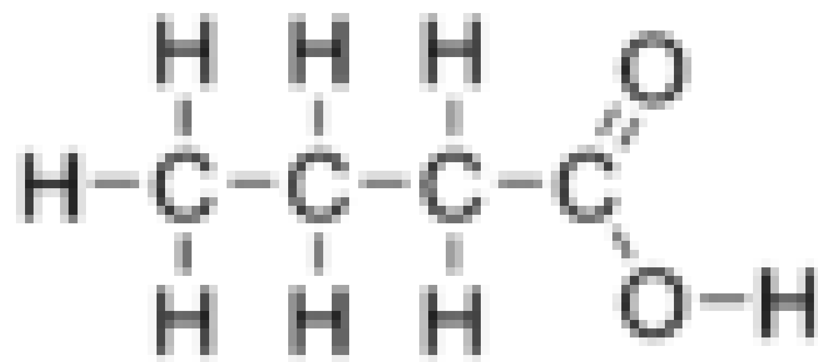
Vinegar is a mixture of water (95%) and acetic acid (5%)





Fatty acids

- Fatty acids are nothing more or less than longer carboxylic acids
- The shortest of biological interest is butanoic acid, better known as butyric acid
- Butyric acid is the carboxylic acid from butane
- It's found in dairy products and makes up about 3-4% of butter, where it is bound as a triglyceride
- Free butyric acid has a very intense, unpleasant odor; it's the dominant smell in vomit



Fatty acids

Naturally occurring fatty acids generally have an even number of carbons

Fatty acids are usually found incorporated into triglycerides (more later)

Short-chain fatty acids are up to 4 carbons, medium-chain FA are 6 to 12, and long-chain FA are longer than 12 up to 21.

Many fatty acids have common names that were used before the systematic chemical names came into use

Fatty acids may have no double bonds (saturated fats), one double bond (monunsaturated fatty acids) or more than one double bond (polyunsaturated fatty acids)

Lipid number of fatty acids

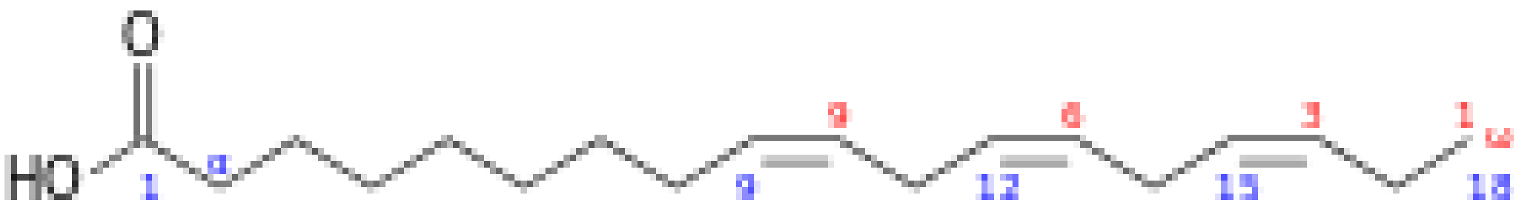
Lipid number is a shorthand for:

- a) the number of carbons in a fatty acid,
- b) the number of double bonds,
- c) the location of the first double bond from the non-acid end

Example: Alpha-linolenic acid (18:3 n-3) has:

- a) 18 carbons,
- b) 3 double bonds,
- c) first double bond at the third carbon from the non-acid end

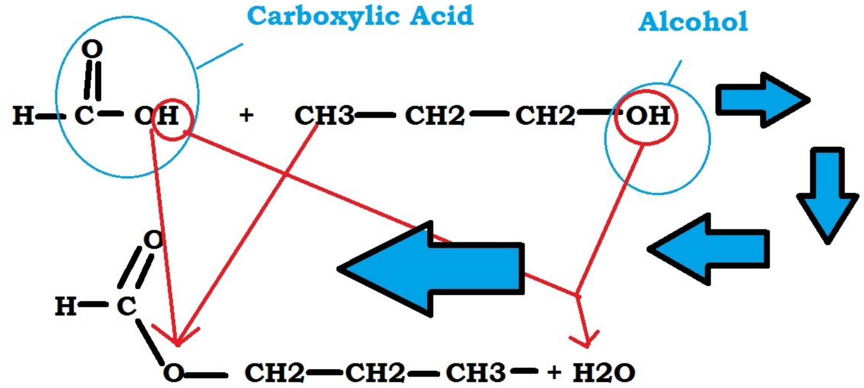
The location of the double bond, designated n-3, is also referred to as “omega-3”, or “ω-3”; these are spoken as “n minus three” and “omega minus three”, though the “minus” is often left out in casual speech



Esterification

Carboxylic acid combines with an alcohol to form an ester

The hydroxyl (-OH) from the alcohol joins the hydrogen from the carboxylic acid to make H_2O, and the remaining parts of the two original molecules bond to form a single molecule



*Basically the OH from the Caroxylic Acid joins with the OH in the Alcohol forming H2O and the oxygen left over bonds with the carbon group in the alchol. This process is called Esterification.

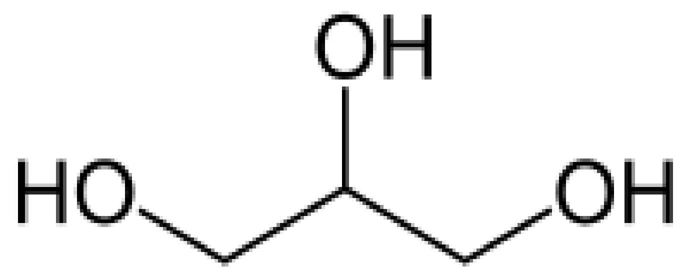
Glycerol

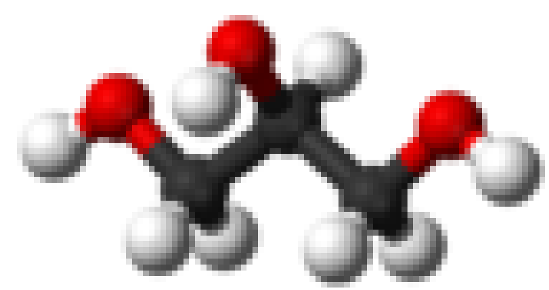
Glycerol, perhaps more familiar by its common name "glycerin", is a poly-alcohol, or polyol

- Propane-1,2,3-triol

Based on propane, each carbon has an hydroxyl group

Serves as the backbone of a triglyceride, formed by attaching fatty acids at the hydroxyl locations by their acid end through a reaction called esterification





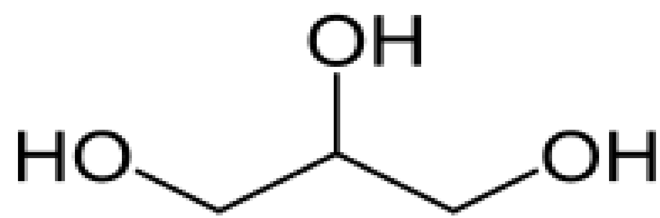
Esterification of FA and glycerol

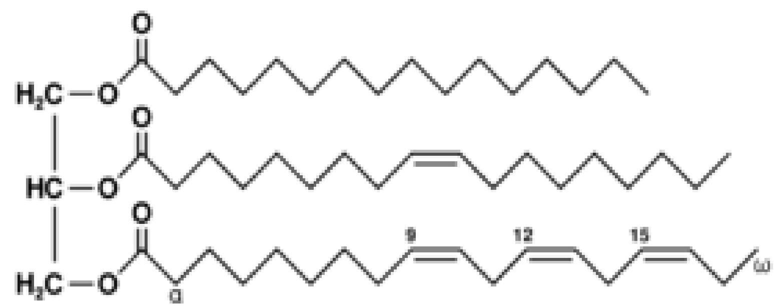
A reaction that brings together an alcohol and an acid

Take out H_2O and link the remaining ends

R-CO-O-R

Glycerol can esterify with three fatty acids to make a triglyceride





Why esterify?

"Defang" the carboxylic acid (CA)

- Tie up the reactive -COO part of CA

The resulting triglyceride has no remaining strong polar groups

- No longer mixes with water
- Triglyceride molecules will aggregate with one another for compact storage, taking up less room
- Relatively inert and non-reactive, until needed

Splitting triglycerides - lipases

When and where fatty acids are needed, an enzyme called *lipase* is present to split the triglyceride into fatty acids plus glycerol

Triglycerides are carried to muscles in lipoprotein particles to provide energy

- Lipoprotein lipase in the blood vessel wall liberates fatty acid from triglyceride, allowing it to enter the muscle cell

Triglycerides and fatty acids

So, triglycerides and fatty acids are closely related

- Triglycerides are formed from fatty acids plus glycerol by esterification
- Triglyceride is the practical storage and transport form of fatty acids
- However, at each stage of transport and storage, triglyceride must be broken down to fatty acids

Triglycerides = fatty acids

Often as we discuss fatty acids, for example, the fatty acid content of different foods, it will be taken for granted that they are actually present there as a triglyceride

Fatty acids - Overview

Saturated fats

- No double bonds

Monounsaturated fatty acids

- One double bond

Polyunsaturated fatty acids

- More than one double bond

PUFA

Polyunsaturated fatty acid

- More than one double bond

PUFA are essential fatty acids (EFA)

- Like vitamins, EFA are required but cannot be synthesized in humans

Plant-derived

- Linoleic acid (LA) n-6
- Alpha-linolenic acid (ALA) n-3

Marine-derived

- Docosahexaenoic acid (DHA) n-3
- Eicosapentaenoic acid (EPA) n-3

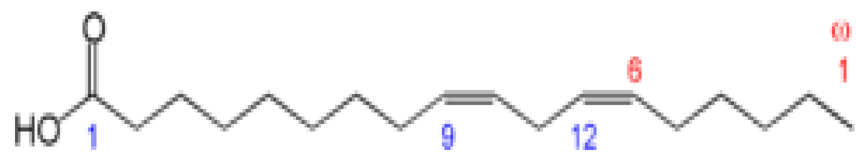
LA - Plant n-6 PUFA

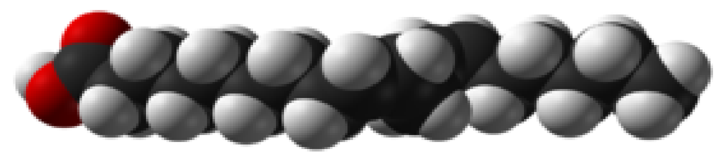
Linoleic acid (18:2 n-6)

Substantial amounts in many food sources – seeds, nuts, vegetable oils, egg yolks

Makes up much of the fat content of the current U.S. diet as a replacement for saturated fats, resulting in lower blood cholesterol levels

Essential fatty acid, required for synthesis of arachidonic acid, cell membranes





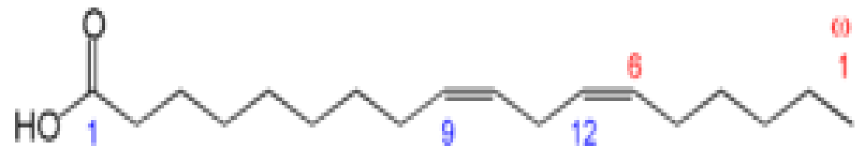
LA - Plant n-6 PUFA

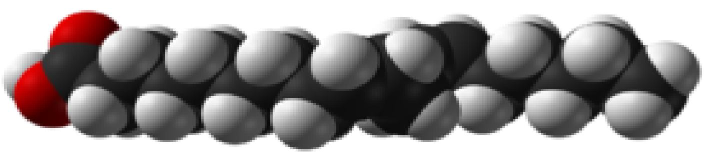
Linoleic acid (18:2 n-6)

Controversy regarding the optimal amount of LA to include in the diet

- Some authorities say upper limit should be about 10 g/d, else adverse health consequences expected
- Others believe that lowering dietary LA would be detrimental, because LA helps to reduce LDL levels

We have a winner - all will be revealed!





ALA – Plant n-3 PUFA

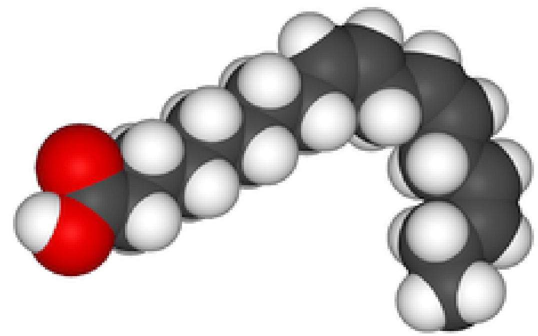
Alpha-linolenic acid (18:3 n-3)

Substantial amounts in flax, chia, walnuts, and vegetable oils (soybean, canola)

Essential fatty acid – intake of 2-3 g/d recommended

Possible protective effect against CHD

Converted into EPA and DHA n-3 PUFA in the body, though rate is slow



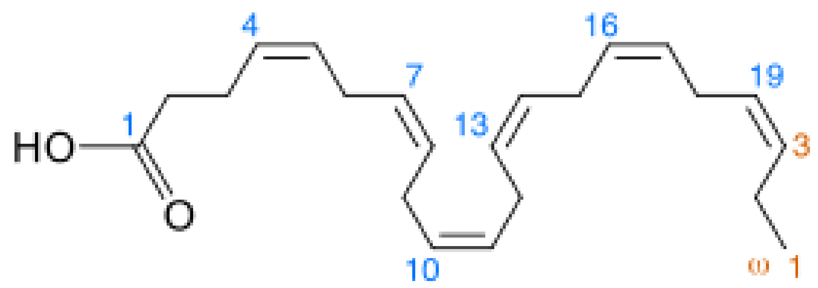
DHA - Marine n-3 PUFA

Docosahexaenoic acid (22:6 n-3)

Found in high concentration in fatty fish, less in lean fish and shellfish, along with EPA

Primary component of brain, retina, testes; essential for brain development

Synthesized *in vivo* from alpha-linolenic acid, at low rates



EPA – Marine n-3 PUFA

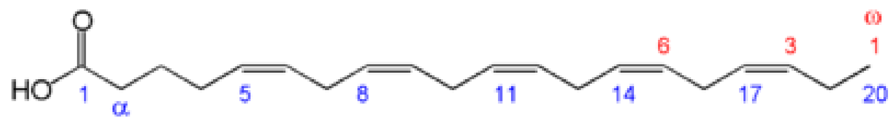
Eicosapentaenoic acid (20:5 n-3)

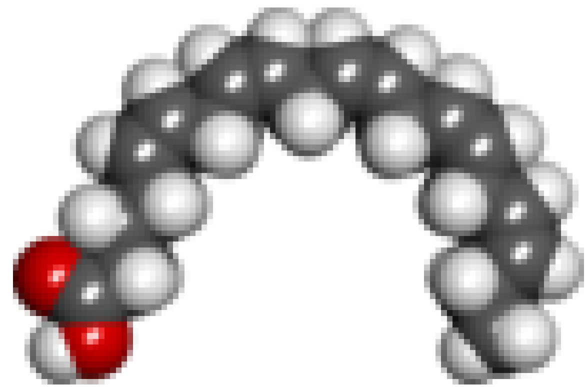
Found in high concentration in fatty fish, less in lean fish and shellfish, along with DHA

Inhibits platelet aggregation

Reduces inflammation

Synthesized *in vivo* from alpha-linolenic acid, at low rate



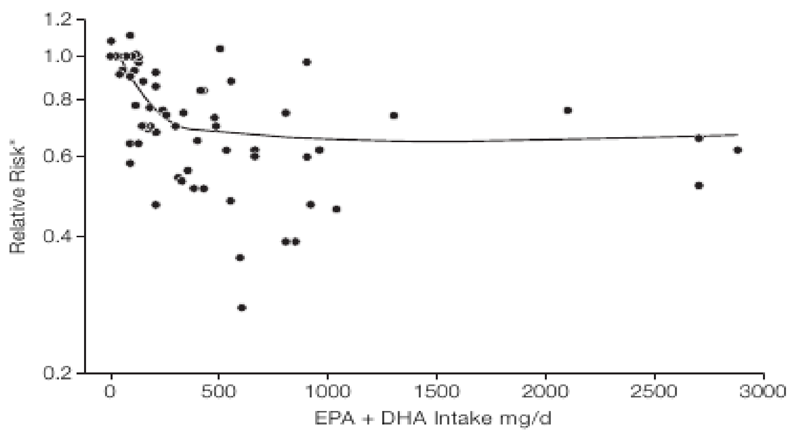


DHA + EPA – Marine n-3 PUFA

Consumption of cold water, fatty fish provides (relatively) large amounts of DHA + EPA

Epidemiologic studies find strong correlation of high DHA+EPA consumption with lower cholesterol levels and lower CHD incidence / death; optimum 250-1000 mg/d

Figure 2. Relationship Between Intake of Fish or Fish Oil and Relative Risks of CHD Death in Prospective Cohort Studies and Randomized Clinical Trials



The Fog of PUFA

Often, PUFAs are lumped together as if they were one entity

- Nutrition Facts food labels, for instance
- This implies that you need not consider them separately, which was the earlier belief
- Current understanding is to separate into n-6, plant n-3 and marine n-3

Often, the n-3 ("omega-3") fatty acids are lumped together

- Marine and plant n-3 are related but not interchangeable

Results of clinical trials and observational studies may be difficult to interpret, due to insufficient specificity of PUFA

MUFA

Monounsaturated fatty acids

- Oleic acid (18:1 n-9)
  - Prominent in olive oil and other vegetable oils, seeds and nuts
  - Nutrient fatty acid, used as general purpose fuel and substrate in the body
  - Lowers LDL when substituted for saturated fat
- Palmitoleic acid (16:1 n-7)
  - Prominent in macadamia nut oil, other vegetable oils
  - Nutrient fatty acid; common in human fatty tissue and liver
  - Potential role is signaling re: obesity

MUFA potentially useful replacements for saturated fats in regard to lowering cholesterol and/or lowering CHD risk

- Earlier studies were inconclusive
- Better data now

Saturated fats

Dietary fatty acids, making up the bulk of fats in the typical American diet in the 20th century

Generally considered as a homogeneous group in regard to their biological effects, including tendency to raise blood cholesterol and triglyceride levels

Butyric acid (4:0) - contained in butter

Lauric acid (12:0) - contained in coconut oil, palm kernel oil, and breast milk

Myristic acid (14:0) - contained in cow's milk and dairy products

Palmitic acid (16:0) - contained in palm oil and meat

Stearic acid (18:0) - contained in meat and cocoa butter

Recent advice on dietary fats

Reduce saturated fat intake to 10% of energy (25 g/d)

Favor polyunsaturated fat intake: marine n-3 250-1000 mg/d, plant n-3 (ALA) 2-3 g/d, and remainder PUFA (mostly LA) up to 20 g/d

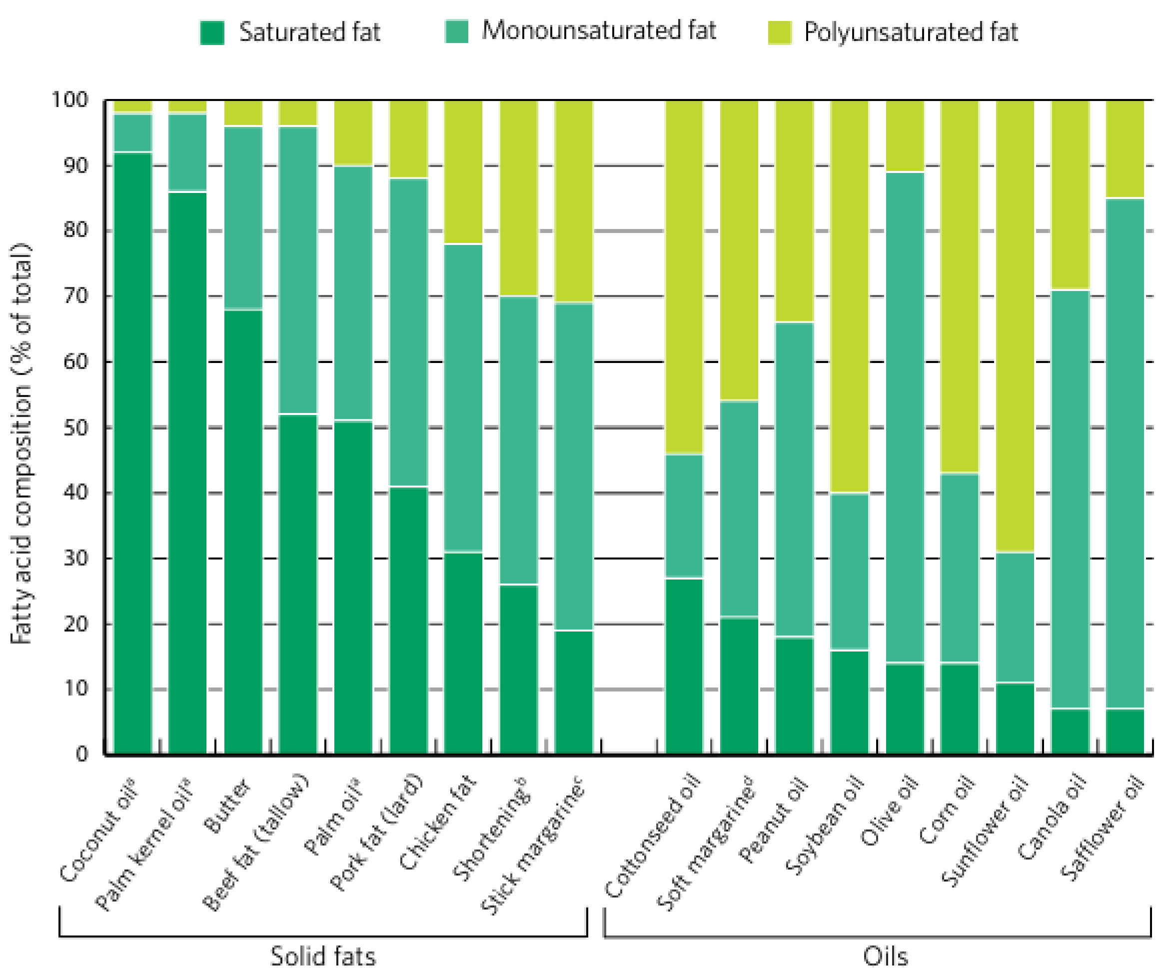
Monounsaturated to bring total fats to 70-80 g/d

Fat content of nuts

Table 1. Average nutrient composition of nuts (per 100 g).

Nuts	Energy (kJ)	Fat (g)	SFA (g)	MUFA (g)	PUFA (g)	LA (g)	ALA (g)	Protein (g)	Fiber (g)	Folate (µg)	PS (mg)
Almonds	2418	50.6	3.9	32.2	12.2	12.2	0.00	21.3	8.8	29	120
Brazil nuts (dried)	2743	66.4	15.1	24.5	20.6	20.5	0.05	14.3	8.5	22	NR
Cashews	2314	46.4	9.2	27.3	7.8	7.7	0.15	18.2	5.9	25	158
Hazelnuts	2629	60.8	4.5	45.7	7.9	7.8	0.09	15.0	10.4	113	96
Macadamia nuts	3004	75.8	12.1	58.9	1.5	1.3	0.21	7.9	6.0	11	116
Peanuts	2220	49.2	6.8	24.4	15.6	15.6	0.00	25.8	8.5	145	220
Pecans	2889	72.0	6.2	40.8	21.6	20.6	1.00	9.2	8.4	22	102
Pine nuts (dried)	2816	68.4	4.9	18.8	34.1	33.2	0.16	13.7	3.7	34	141
Pistachios	2332	44.4	5.4	23.3	13.5	13.2	0.25	20.6	9.0	51	214
Walnuts	2738	65.2	6.1	8.9	47.2	38.1	9.08	15.2	6.4	98	72

FIGURE 3-3. Fatty Acid Profiles of Common Fats and Oils



Mortality: Fats vs. Carbs

Association of Specific Dietary Fats With Total and Cause-Specific Mortality

Dong D. Wang, MD, MSc; Yanping Li, PhD; Stephanie E. Chiuve, ScD; Meir J. Stampfer, MD, DrPH; JoAnn E. Manson, MD, DrPH; Eric B. Rimm, ScD; Walter C. Willett, MD, DrPH; Frank B. Hu, MD, PhD

JAMA Internal Med. 2016

Mortality: Fats vs. Carbs

NHS

- Subjects: 83,349
- Events: 20,314 (deaths)
- Follow up: 32 yrs

HPFS

- Subjects: 42,884
- Events: 12,990 (deaths)
- Follow up: 26 yrs

Factors:

- Age, race, marital status, BMI, physical activity, smoking, alcohol, vitamin use, aspirin use, family history (CHD, DM, Ca), personal history (Htn, lipids), menopause, HRT
- Dietary (FFQ including macronutrients, cholesterol)

Mortality: Fats vs. Carbs

Total fats (TF)

Trans fats (TransF)

Saturated fats (SFA)

Unsaturated fats (UFA)

- Monounsaturated fats (MUFA)
- Polyunsaturated fats (PUFA)
  - ω-6 (LA, AA)
  - ω-3 (ALA)
  - ω-3 (EPA+DHA)

Mortality: Fats vs. Carbs

Factors by increasing amount of SFA and MUFA consumed

- More total energy consumed
- Less carbs consumed
- Less alcohol consumed
- Less physical activity
- Greater likelihood of smoking

Factors that differed by increasing fat intake generally associated with worse prognosis

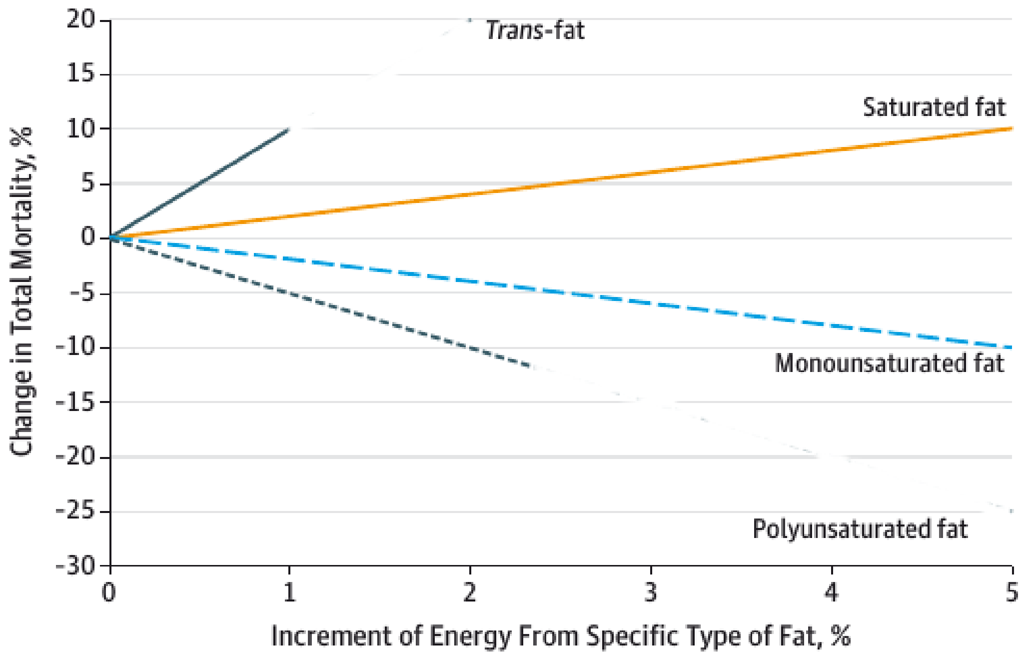
Total mortality: Fats vs. Carbs

Component	Unadjusted HR	Adjusted HR	Q1-Q5 (% cal)
Total Fat	1.29	0.84	24-40%
Saturated Fat	1.71	1.08	8-15%
Unsaturated Fat	1.03	0.76	14-23%
Polyunsaturated Fat	0.73	0.81	4.3-7.6%
Monounsaturated Fat	1.22	0.89	9-16%
Omega-6 PUFA (LA, AA)	0.75	0.85	3.5-6.8%
Omega-3 PUFA (ALA)	0.79	0.99	0.4-0.7%
Omega-3 PUFA (DHA, EPA)	0.74	0.96	0.04-0.25%
Trans-fats	1.73	1.13	0.8-2.2%

HR reflects comparison when the highest quintile of that fat intake is substituted for the same # calories of carbohydrates

Total mortality: Fats vs. Carbs

Figure 1. Change in Total Mortality Associated With Increases in the Percentage of Energy From Specific Types of Fat

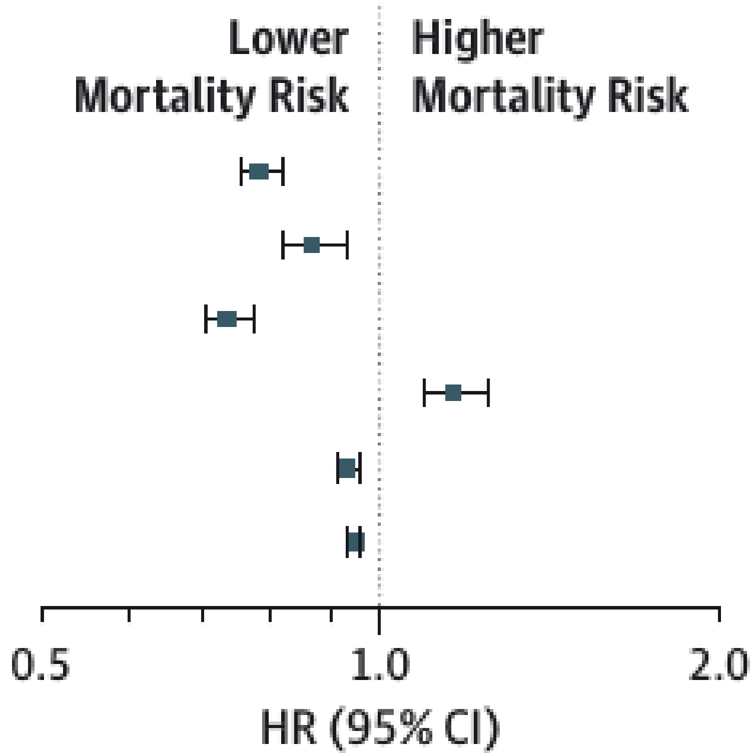


Multivariable hazard ratios of total mortality associated with replacing the percentage of energy from total carbohydrates by the same energy from specific types of fat (*P* < .001 for trend for all) were used. The model was

Total mortality: Fat vs. SF

A Total mortality

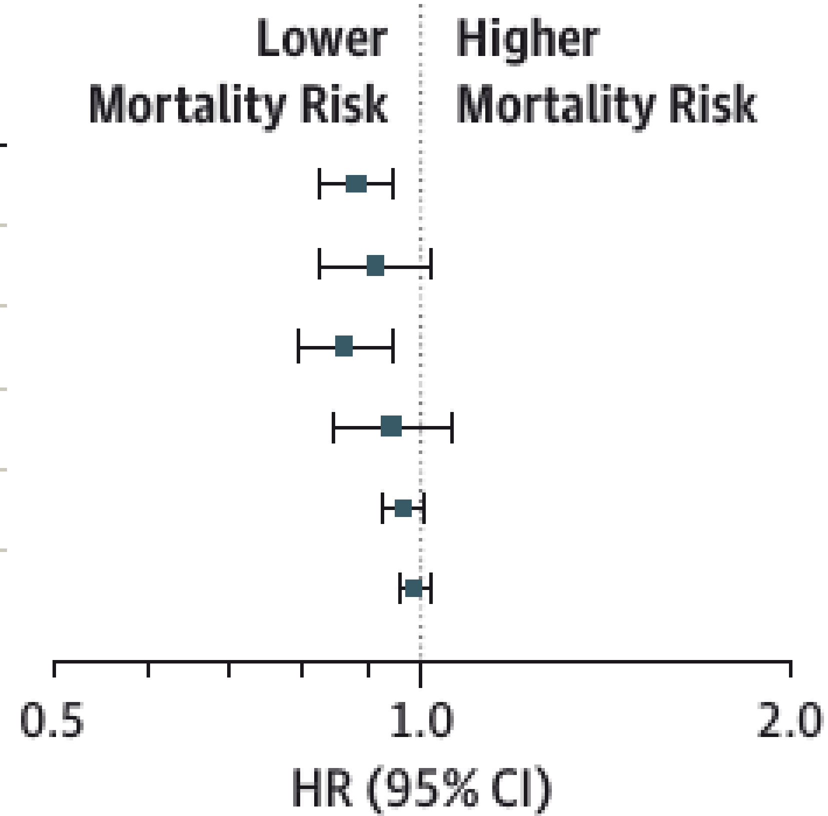
	HR (95% CI)
UFAs, 5% of energy	0.78 (0.75-0.82)
MUFAs, 5% of energy	0.87 (0.82-0.93)
PUFAs, 5% of energy	0.73 (0.70-0.77)
Trans-fat, 2% of energy	1.16 (1.09-1.24)
ω-6 PUFAs, 2% of energy	0.93 (0.91-0.96)
ω-3 PUFAs, 0.3% of energy	0.95 (0.93-0.96)



Cancer mortality: Fat vs. SF

C Cancer mortality

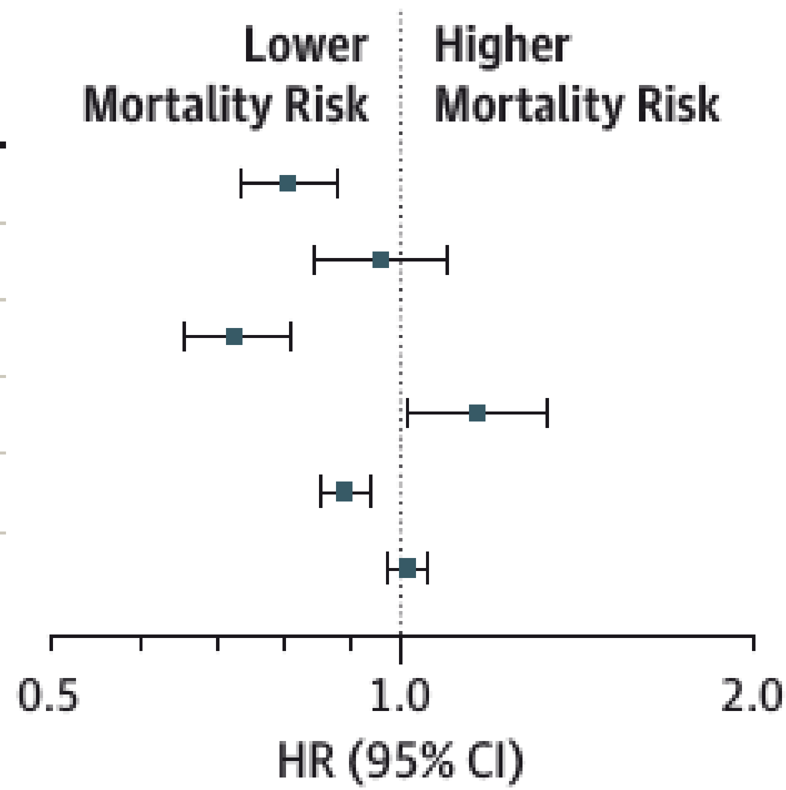
	HR (95% CI)
UFAs, 5% of energy	0.88 (0.82-0.94)
MUFAs, 5% of energy	0.91 (0.82-1.01)
PUFAs, 5% of energy	0.86 (0.79-0.94)
Trans-fat, 2% of energy	0.94 (0.84-1.05)
ω-6 PUFAs, 2% of energy	0.96 (0.92-1.00)
ω-3 PUFAs, 0.3% of energy	0.98 (0.95-1.01)



Cardiovasc mortality: Fat vs. SF

B Cardiovascular disease mortality

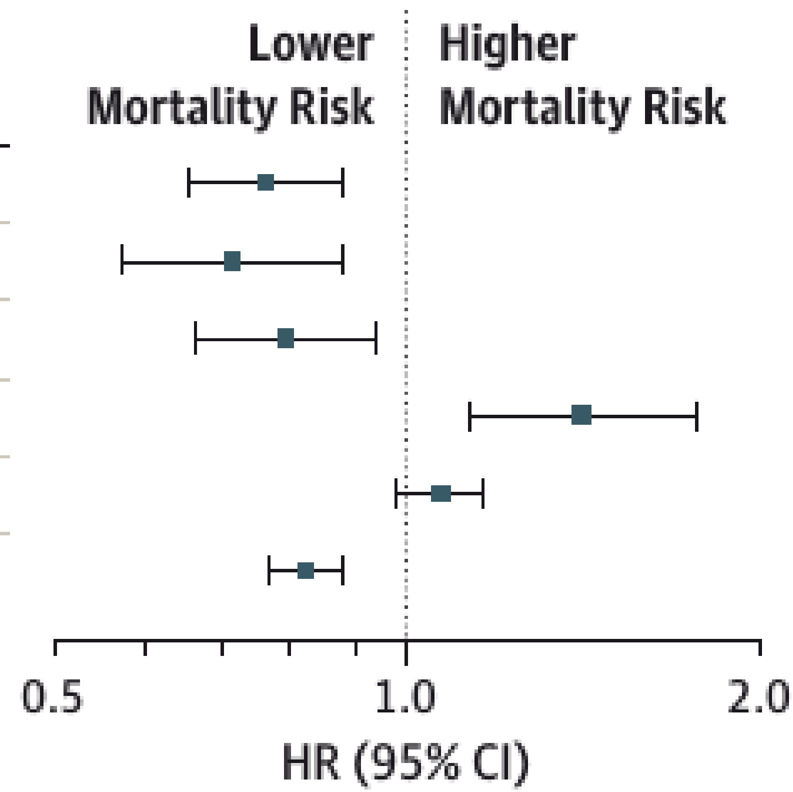
	HR (95% CI)
UFAs, 5% of energy	0.80 (0.73-0.88)
MUFAs, 5% of energy	0.96 (0.84-1.09)
PUFAs, 5% of energy	0.72 (0.65-0.80)
Trans-fat, 2% of energy	1.16 (1.01-1.33)
ω-6 PUFAs, 2% of energy	0.89 (0.85-0.94)
ω-3 PUFAs, 0.3% of energy	1.01 (0.97-1.05)



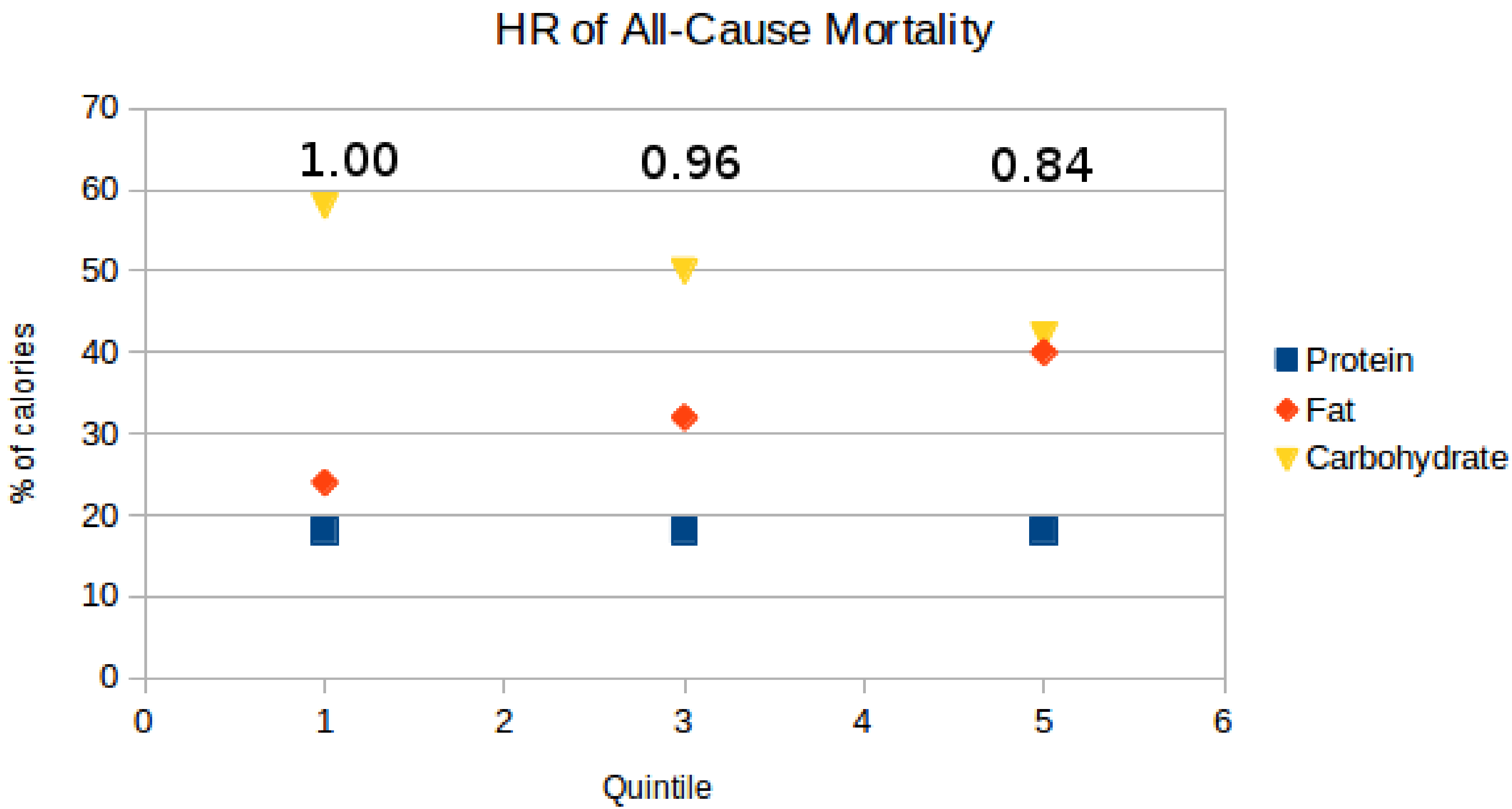
Neuro mortality: Fat vs. SF

D Neurodegenerative disease mortality

	HR (95% CI)
UFAs, 5% of energy	0.76 (0.65-0.88)
MUFAs, 5% of energy	0.71 (0.57-0.88)
PUFAs, 5% of energy	0.79 (0.66-0.94)
Trans-fat, 2% of energy	1.41 (1.13-1.76)
ω-6 PUFAs, 2% of energy	1.07 (0.98-1.16)
ω-3 PUFAs, 0.3% of energy	0.82 (0.76-0.88)



NHS/HPFS Fats & Mortality



NHS/HPFS Fats & Mortality

Carbohydrates offer a slight advantage over saturated fats in calorie-for-calorie exchange

However, consuming larger amounts of monounsaturated and polyunsaturated fats is better than either SF or carb

The best strategy appears to be aiming for 40% fat, with the majority (2/3) coming from mono- and polyunsaturated FA

Remaining calories come from 42% carbs and 18% protein

My Takeaway on Fat Intake (1)

Fish oil, other PUFA, MUFA supplements

- Get definite benefit from PUFA in food, rather than questionable benefit from supplement
- BUT strongly consider taking supplement if recommended by your personal MD

My Takeaway on Fat Intake (2)

Eat fish and plant sources to get adequate dietary ω-3 (omega-3) PUFA and associated micronutrients

- Two servings per week of salmon, tuna, or other high ω-3 type (250 mg/d ω-3)
- 2-3 g/d of *ALA* (alpha-linolenic acid) from seeds, nuts, oils

My Takeaway on Fat Intake (3)

Seek out omega-6 PUFA (linoleic acid) in vegetable oils and spreads

- Controversy over its potential adverse cardiovascular effects has been settled
- 7% of calories is reasonable target (14 g/d)

My Takeaway on Fat Intake (4)

Be strategic regarding dietary saturated fat

- Saturated fat comes largely from red meat / processed meat, which should be consumed sparingly based on other evidence
- Dairy products in reasonable amounts are OK
- Don't shun nuts and seeds just because of saturated fat content
- Choose vegetable oils with lower SF
- Limit SF to 10% of calories (20 g/d)

My Takeaway on Fat Intake (5)

Dietary MUFAs round out total fat intake

- 15-20% of calories (30-40 g/d)
- Olive oil especially

Total fat intake of 35-40% of energy (calories) is desirable

- Example: If total Calories is 1800, fat is 720 Calories or 80 g (since 9 Cal/g fat)

Fat Finale

Dietary fat is not the pariah, contrary to what we were taught for decades

- We do not become obese or sick as a result of excessive dietary fat
- In fact, the exact opposite is observed

We would do well to eat more fat than is customary, in place of carbohydrates

- Granted, of course, that we favor fats with the desirable outcomes (PUFA, MUFA) and *go* easy on the others (SF, transF, and foods containing them, especially red meats and processed meats)